

REMARKS

Applicants have amended claims 1, 2, 46, 47, 52, and 65. Support for these amendments can be found in the original claims and in the Specification. Claims 1-14, 16, 17, 22-25, 30-36, and 38-66 are currently pending. Reconsideration of the pending application is respectfully requested in view of the following remarks.

Rejections Under 35 U.S.C. § 112

Claims 1-14, 16, 17, 22-25, 30-36, and 38-66 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants have addressed each of the typographical errors identified by the examiner. See subparagraphs 4a-c, e-l, n, p and q in the Office Action at pages 3-4. With respect to the phenyl substituents, the phrase "at each occurrence, phenyl is optionally substituted with..." modifies all the substituents of formula I that contain a phenyl moiety, e.g., R₆ and R₇. See subparagraphs 4d and 4m of the Office Action. Claims 1 and 47 have been amended to supply antecedent basis for -CH₃ and -CF₃ as possible phenyl substituents. See claims 19 and 58. Reconsideration of these rejections is respectfully requested in view of the foregoing amendments and remarks.

CONCLUSION

Claims 1-14, 16, 17, 22-25, 30-36, and 38-66 are now in condition for allowance, which action is respectfully request. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,



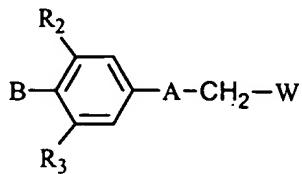
Jonathan P. O'Brien, Patent Agent
Registration No. 50,852

Date: July 24, 2002

Pharmacia & Upjohn Company
Global Intellectual Property
301 Henrietta Street
Kalamazoo, Michigan 49001
Telephone No. (269) 833-2102 or (269) 833-9500
Telefax No. (269) 833-8897 or (269) 833-2316

Version with markings to show changes made

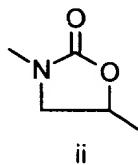
1. A compound of formula I



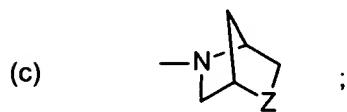
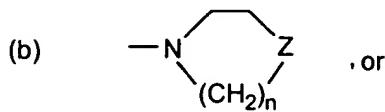
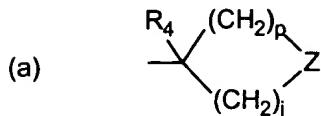
I

or a pharmaceutically acceptable salt thereof wherein:

A is a structure ii



B is



W is NHC(=X)R₁, or -Y-het; [provided that when A is a structure iv, W is not -Y-het;]

X is O, or S; provided that when X is O, B is not the subsection (b)[.];

Y is NH, O, or S;

Z is S(=O)(=N-R₅);

R₁ is

(a) H,

- (b) NH₂,
- (c) NHC₁₋₄alkyl,
- (d) C₁₋₄alkyl,
- (e) C₂₋₄alkenyl,
- (f) OC₁₋₄alkyl,
- (g) SC₁₋₄alkyl, or
- (h) (CH₂)_pC₃₋₆cycloalkyl;

at each occurrence, alkyl or cycloalkyl in R₁ is optionally substituted with one or more F, Cl or CN;

R₂ and R₃ are independently H, F, Cl, methyl or ethyl;

R₄ is H, CH₃, or F;

R₅ is

- (c) C(=O)C₁₋₄alkyl,
- (d) C(=O)OC₁₋₄alkyl,
- (e) C(=O)NHR₆, or
- (f) C(=S)NHR₆;

R₆ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, alkyl in R₅ and R₆ is optionally substituted with one or more halo, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, [C(=O)R'] C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, NR₇R₇, oxo, or oxime; R₇ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, phenyl is optionally substituted with one or more halo, CF₃, CH3, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, [C(=O)R'] C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, or NR₇R₇;

het is a C-linked five- (5) membered heteroaryl ring having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen, or het is a C-linked six (6) membered heteroaryl ring having 1-3 nitrogen atoms;

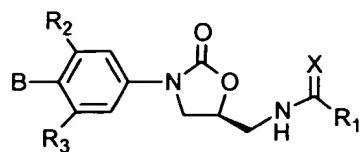
p is 0, 1, or 2;

j is 1, 2, 3, 4, or 5; provided that [k and j] j and p taken together are 2, 3, 4 or 5;

m is 0, 1, or 2;

n is 2 or 3; and ---- in structure iii is either a double bond or a single bond.

2. A compound of [formula I which is a compound of formula IA:] claim 1 having the formula IA:



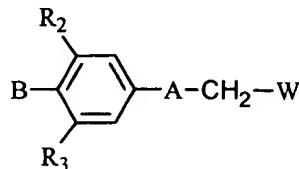
IA.

46. A compound of claim 2 which is

N-((5S)-3-[3-fluoro-4-[1-(acetylimino)-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)acetamide, Z-isomer;
N-((5S)-3-[3-fluoro-4-[1-(acetylimino)-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer;
N-((5S)-3-[3-fluoro-4-(1-[(methylamino)carbonyl]imino)-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer;
N-((5S)-3-[3-fluoro-4-(1-[(methoxycarbonyl)imino]-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer;
N-((5S)-3-[3-fluoro-4-(1-[(ethoxycarbonyl)methyl]imino)-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer;
N-((5S)-3-[3-fluoro-4-(1-[[[4-nitrophenyl]amino]carbonyl]imino)-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer ;
N-((5S)-3-[3-fluoro-4-[1-[(aminocarbonyl)imino]-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer;
N-((5S)-3-[3-fluoro-4-[1-[[aminocarbonyl)methyl]imino]-1-oxohexahydro-1λ⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide, Z-isomer;

N-[((5*S*)-3-{3-fluoro-4-(1-[(methoxycarbonyl)imino]-1-oxido-1 λ^4 , 4-thiazinan-4-yl)phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]propanethioamide;
N-[((5*S*)-3-{3-fluoro-4-(1-[(methoxycarbonyl)imino]-1-oxido-1 λ^4 , 4-thiazinan-4-yl)phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]cyclopropanecarbothioamide ;
N-[((5*S*)-3-{3-fluoro-4-[1-[(methoxycarbonyl)imino]-1-oxidohexahydro-1 λ^4 -thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl] cyclopropanecarbothioamide, Z-isomer;
N-[((5*S*)-3-{3-fluoro-4-[1-[[phenylmethoxy][carbonyl]carbonyl]imino]-1-oxidohexahydro-1 λ^4 -thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide, Z-isomer; or
N-((5*S*)-3-[3-[Fluoro] fluoro-4-(1-[(benzylamino)carbonyl]imino)-1-oxidohexahydro-1 λ^4 -thiopyran-4-yl]phenyl)-2-oxo-1,3-oxazolidin-5-yl)methyl)acetamide, Z-isomer.

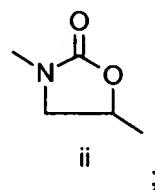
47. 1. A compound of formula II



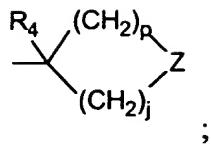
II

or a pharmaceutically acceptable salt thereof wherein:

A is a structure ii



B is

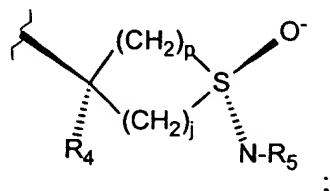


W is $NHC(=X)R_1$, or $-Y\text{-het}$; [provided that when A is a structure iv, W is not $-Y\text{-het}$;]

X is O, or S; [provided that when X is O, B is not the subsection (b).]

Y is NH, O, or S;

Z is $S(=O)(=N-R_5)$ and the B ring has the following stereochemistry



R_1 is

- (a) H,
- (b) NH_2 ,
- (c) $NHC_{1-4}\text{alkyl}$,
- (d) $C_{1-4}\text{alkyl}$,
- (e) $C_{2-4}\text{alkenyl}$,
- (f) $OC_{1-4}\text{alkyl}$,
- (g) $SC_{1-4}\text{alkyl}$, or
- (h) $(CH_2)_p C_{3-6}\text{cycloalkyl}$;

at each occurrence, alkyl or cycloalkyl in R_1 is optionally substituted with one or more F, Cl or CN;

R_2 and R_3 are independently H, F, Cl, methyl or ethyl;

R_4 is H, CH_3 , or F;

R_5 is

- (a) H,
- (b) $C_{1-4}\text{alkyl}$,
- (c) $C(=O)C_{1-4}\text{alkyl}$,
- (d) $C(=O)OC_{1-4}\text{alkyl}$,

- (e) C(=O)NHR₆, or
- (f) C(=S)NHR₆;

R₆ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, alkyl in R₅ and R₆ is optionally substituted with one or more halo, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, [C(=O)R⁷] C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, NR₇R₇, oxo, or oxime; R₇ is H, C₁₋₄alkyl, or phenyl;

at each occurrence, phenyl is optionally substituted with one or more halo, CF₃, CH₃, CN, NO₂, phenyl, C₃₋₆ cycloalkyl, OR₇, [C(=O)R⁷] C(=O)R₇, OC(=O)R₇, C(=O)OR₇, S(=O)_mR₇, S(=O)_mNR₇R₇, NR₇SO₂R₇, NR₇SO₂NR₇R₇, NR₇C(=O)R₇, C(=O)NR₇R₇, or NR₇R₇;

het is a C-linked five- (5) membered heteroaryl ring having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen, or het is a C-linked six (6) membered heteroaryl ring having 1-3 nitrogen atoms;

p is 0, 1, or 2;

j is 1, 2, 3, 4, or 5; provided that **[k and j] j and p** taken together are 2, 3, 4 or 5;

m is 0, 1, or 2;

[n is 2 or 3;] and ---- in structure iii is either a double bond or a single bond..

52. The compound of claim 47 wherein R₁ is cyclopropyl.

65. A compound of claim 47 which is

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)acetamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)ethanethioamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)propanethioamide (Z)-isomer;

N-((5S)-3-[3-fluoro-4-(1-imino-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)cyclopropanethioamide (Z)-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-(acetylmino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-(methylmino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-(acetylmino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-(ethylmino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-[(phenylmethyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-[(3-phenylpropyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-(1-{[(methylamino)carbonyl]imino}-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-(1-[(methoxycarbonyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-(1-[(ethoxycarbonyl)methyl]imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-(1-{{[[4-nitrophenyl]amino]carbonyl]imino}-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer ;

N-((*(5S*)-3-[3-fluoro-4-[1-[(aminocarbonyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-{{[(aminocarbonyl)methyl]imino}-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-[(2-hydroxyethyl)imino]-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)propanethioamide, *Z*-isomer;

N-((*(5S*)-3-[3-fluoro-4-[1-(methylmino)-1-oxidohexahydro-1*λ*⁴-thiopyran-4-yl]phenyl]-2-oxo-1,3-oxazolidin-5-yl}methyl)cyclopropanecarbothioamide, *Z*-isomer;

N-[((5*S*)-3-{3-fluoro-4-[1-[(methoxycarbonyl)imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]cyclopropanecarbothioamide, *Z*-isomer;

N-[((5*S*)-3-{3-fluoro-4-[1-[[phenylmethoxy][carbonyl]carbonyl]imino]-1-oxidohexahydro-1λ⁴-thiopyran-4-yl]phenyl}-2-oxo-1,3-oxazolidin-5-yl)methyl]acetamide, *Z*-isomer; or

N-((5*S*)-3-[3-[**Fluoro**] **Fluoro**-4-(1-[(benzylamino)carbonyl]imino)-1-oxidohexahydro-1λ⁴-thiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl)methyl)acetamide, *Z*-isomer.